DEC 2 3 2003

K032113/S1

510(k) Summary of Substantial Equivalence
ChromaVision Medical Systems, Inc.
(Automated Cellular Imaging System)

This summary of substantial equivalence information is furnished in accordance with 21 CFR 807.92 as follows:

21 CFR 807.92(a):

21 CFR 807.92(a)(1):

* Submitter's name and address:

ChromaVision Medical Systems, Inc.
33171 Paseo Cerveza
San Juan Capistrano, California
92675

* Submitter's telephone number: (949) 443-3355

* Contact person:

Mr. David G Davis
ChromaVision Medical Systems, Inc.
33171 Paseo Cerveza
San Juan Capistrano, California
92675

* Date this 510(k) summary was prepared: June 30, 2003.

21 CFR 807.92(a)(2):

* Trade/proprietary name of the device: ACIS (Automated Cellular Imaging System)

* Classification name: Automated microscopy cell locating workstation

21 CFR 807.92(a)(3): Legally marketed predicate devices to which substantial equivalence is claimed:

510(k) Summary of Substantial Equivalence
ChromaVision Medical Systems, Inc.
(Automated Cellular Imaging System)

* ChromaVision Medical Systems, Inc. ACIS – ER/PR SW Application

* Human manual visualization by conventional microscopy

21 CFR 807.92(a)(4): Description of the device that is the subject of this premarket notification:

System Introduction
The ACIS is a highly automated microscope and software system capable of operating continuously with limited human supervision and maintenance. By automating certain steps of the basic microscopic procedure (loading, positioning, focusing, scanning, and cell identification and quantification), the ACIS can significantly improve the consistency, speed, reproducibility, and accuracy of traditional manual or semi-manual laboratory results.

The ACIS can automatically scan and process up to 100 slides while operating unattended. As each slide is processed, the system automatically stores individual fields of view in order to map and integrate this into a single image, a histological reconstruction of the entire tissue section. The proprietary software-based digital color detection technology offers significant sensitivity and specificity to identify targeted cells using common laboratory stains. This technology utilizes advanced imaging concepts referred to as "color spaces" and "color space conversion."

Overview of System Operation
During normal operation, a laboratory technician mounts prepared microscope slides onto a specially designed slide carrier which has the capacity to hold up to four slides. Up to 25 slide carriers can be loaded into the ACIS slide transport system, for a "run" throughput of 100 slides. The scanning process begins with the automatic loading of the first carrier of slides onto the microscope stage. During this stage of the process, the ACIS automatically reads bar codes affixed to the slides to facilitate participant data storage and access. During scanning, the ACIS automatically focuses each field of view, images the object using the CCD camera, and processes the resulting digital image through the image processor. Slides are then scanned at a low optical magnification (typically 4X objective) to find regions of interest based primarily on their color, along with size and shape characteristics. The locations of regions are stored until scanning is completed. Once the region of interest containing the specimen is found, a scan of the specimen commences to build a low power image of the specimen (histological reconstruction).

For the HER2 assay, the ACIS creates the histological reconstruction. The pathologist may then visit any area of the scanned tissue section at low or high magnification. The pathologist

electronically selects regions of invasive carcinoma. The scoring is expressed as intensity of brown color within the stained cells in the selected area.

After scanning is completed, the operator is able to view the histological reconstruction of all stored images for interpretation of the detected objects, along with quantitative information, such as the number of objects detected and colorimetric value. Upon completion of this review, a report containing relevant images identified by the pathologist may be printed. Images may be saved on the hard drive or archived to removable media.

Complete details of the ACIS may be found in the ACIS Operator's Manual, available from ChromaVision.

21 CFR 807.92(a)(5): Intended use and labeled indications for use:

Intended Use:
The Automated Cellular Imaging System (ACIS) device is intended to detect, count, and classify cells of clinical interest based on recognition of cellular objects of particular color, size, and shape.

In this software application the ACIS is intended for laboratory use as an accessory to the DakoCytomation HercepTest™ to aid in the detection and semi-quantitative measurement of Her2/neu (c-erbB-2) in formalin-fixed, paraffin embedded normal and neoplastic tissue.

The ACIS is capable of detecting and quantifying regions of clinical interest in immunocytochemically stained material that would otherwise be appropriate for manual visualization by conventional microscopy.

When used with the DakoCytomation HercepTest™, it is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered. The pathologist should verify agreement with the ACIS score.

The ACIS system is an adjunctive computer-assisted methodology to assist the reproducibility of a qualified pathologist in the acquisition and measurement of images from microscopic slides of breast cancer specimens stained for the presence of Her2 receptor protein. The accuracy of the test result depends upon the quality of immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in instructions for DakoCytomation HercepTest™ to assure the validity of the ACIS-assisted Her2

score.

NOTE: All of the patients in the HERCEPTIN® clinical trials were selected using an investigational immunohistochemical clinical trial assay (CTA). None of the patients in those trials were selected using the DakoCytomation HercepTest™. The DakoCytomation HercepTest™ was compared to the CTA on an independent set of samples and found to provide acceptably concordant results. The actual correlation of the DakoCytomation HercepTest™ to HERCEPTIN® clinical outcome has not been established.

21 CFR 807.92(a)(6): Technological characteristics:

The design, construction, energy source, and other characteristics of the ACIS candidate device are considered to be substantially equivalent to the relevant features of the predicate devices. A summary of the technological characteristics of the ACIS candidate device in comparison to those of the predicate devices follows:

* **Method of cell detection:** The same as the predicate devices; i.e., colorimetric pattern recognition by microscopic examination of prepared cells by size, shape, hue, and intensity as observed by an automated computer controlled microscope and/or by visual observation by a health care professional.

* **System components:** The system components comprising the candidate device are substantially equivalent to those in the predicate devices; i.e., computer, microscope, color monitor(s), keyboard, printer, automatic loading and positioning of prepared sample on microscope stage, automatic focusing of microscope, and automatic storage of acquired images.

* **Energy source:** The electrical service is 120 VAC 60 HZ, the same as the predicate devices.

21 CFR 807.92(b): 510(k) summaries for those premarket submissions in which a determination of substantial equivalence is also based on performance data shall contain the following information:

510(k) Summary of Substantial Equivalence
ChromaVision Medical Systems, Inc.
(Automated Cellular Imaging System)

21 CFR 807.92(b)(1): Brief discussion of the non-clinical tests submitted, referenced, or relied upon in this premarket notification submission:

There were no nonclinical tests submitted, referenced, or relied upon in this submission.

21 CFR 807.92(b)(2): Brief discussion of the clinical tests submitted in this premarket notification submission:

1. **Agreement between ACIS and Manual methods of review:**
   Studies were conducted to demonstrate the performance of the ACIS device compared to the manual method of slide examination in the analysis of specimens immunohistochemically stained with the DakoCytomation HercepTest™ Kit for the detection of overexpression of the HER2/*neu* protein. Three pathologists scored 90 specimens on a Tissue Micro Array (TMA) slide. The specimens represented a range of HER2/*neu* staining intensities from 0 to 3+, previously selected by an independent pathologist. Approximately 1/3 of the selected specimens were 0 and 1+, 1/3 of the selected specimens were 2+ and 1/3 of the selected specimens were 3+ HER2 scoring intensities. The scores were determined manually according to DAKO's kit insert provided with the HercepTest kit. To assure blinding, a washout period of one-week occurred between readings, per pathologist. Data were analyzed to determine an estimate of agreement. Raw data was recorded, analyzed, and presented in 4 X 4 tables. There was an overall agreement of 75% between the two different methods of review using the 4-category scale (0, 1+, 2+, 3+).

2. **Within/between reproducibility of the ACIS device:**
   Three pathologists analyzed 60 specimens on a standard light microscope and on a single ACIS device. Each pathologist analyzed each specimen three (3) times each, by both methodologies, at approximately the following representative HER2 staining intensity ranges (by DAKO guidelines):
   Negative (< 1+, 10 cases)
   Low Intensity (1+, 20 cases)
   Medium Intensity (2+, 20 cases)
   High Intensity (3+, 10 cases)

   Between Pathologist Reproducibility Results
   For the manual readings, agreement between the pathologists ranged from 55% to 75%, while ACIS-assisted data shows a pairwise agreement score between the pathologists ranging from 93% to 98%. This data demonstrates that use of the ACIS device provides a greater rate of

inter-pathologist agreement than when using the traditional manual method of review for the 4-category scale.

Within Pathologist Reproducibility Results
The within-pathologist agreement for both manual and ACIS-assisted blinded readings of the same 60 clinical specimens demonstrated that the ACIS device provided a higher consistency rate by a measurement of concordance. The overall manual inter-observer agreement was 85.4% while the overall ACIS inter-observer agreement was 95.3% for the 4-category scale.

Inter-ACIS Reproducibility
One pathologist also analyzed the same cases specified in the above study on three different ACIS instruments. Data showed the results of the Inter-ACIS study showed no significant difference between the scores reported by the three different instruments (p=0.897).

21 CFR 807.92(b)(3): Conclusions drawn from the nonclinical and clinical tests:

Conclusion:

Based on the results of the clinical studies described in this report, it is concluded that the ACIS device is as safe and effective (therefore substantially equivalent) as the predicate devices and it provides the health care professional with an important, clinically relevant tool in the assessment of breast cancer patients for whom Herceptin (Trastuzumab) treatment is being considered.

.... END OF 510(k) SUMMARY...

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 2 3 2003

Mr. David G. Davis
Manager of Regulatory Affairs
ChromaVision Medical Systems, Inc.
33171 Paseo Cerveza
San Juan Capistrano, CA 92675-4824

Re: k032113
Trade/Device Name: ACIS
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistological Reagents and Kits
Regulatory Class: Class II
Product Code: NOT
Dated: October 10, 2003
Received: October 14, 2003

Dear Mr. Davis:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): **K032113**

Device Name: **ACIS**

Indications for Use:

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(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Maria Chan

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

Prescription Use ✓ OR Over-the-Counter Use _____
(Per 21 CFR 801.109)

510(k) 032113

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